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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,025	04/24/2001	Judith Aronhime	1662/52602	6176

26646 7590 09/30/2002

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EXAMINER
HUANG, EVELYN MEI

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 09/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/841,025	Applicant(s) ARONHIME ET AL.	
	Examiner Evelyn Huang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *124-260* is/are pending in the application.

4a) Of the above claim(s) *128-138,143-146,149-160,167-246,259 and 260* is/are withdrawn from consideration.

5)☒ Claim(s) *161-164* is/are allowed.

6)☒ Claim(s) *124-127,139-142,147,148,165,166 and 247-258* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

1. Claims 124-260 are pending. Claims 1-123 have been canceled according to the amendment filed on 7-30-2002.

Election/Restrictions

2. In response to the election/restriction requirement, applicant has elected Form D monohydrate. Applicant has canceled claims 1-123 and submitted new claims 124 to 260. Applicant has requested the solvate of form D be included in the examination. Accordingly, solvate of form D is included in the elected Group II. The groups are redefined as follows. The process claims for making the particular Form A, C to H, L are placed in separate groups. Process claims having the same scope as the allowed compound would be rejoined upon allowance of the compound.

I. Claims 151, 155-160, and claims 149-50, 152-154, 247-258 in part, drawn to anhydrous Zolpidem hemitartrate Form C, its composition, and method of use.

Ia. Claim 230, drawn to a process of making Form C.

II. Claims 126-127, 142, 161-166 and claims 124, 125, 139-141, 143, 147, 148, 247-258 in part, drawn to Zolpidem hemitartrate Form D, its composition, and method of use.

IIa. Claims 223-229, 231, drawn to the process of making Form D.

III. Claims 131,133, 135, 136, 167-172, and claims 124, 132, 134, 139-140, 247-258 in part, drawn to Zolpidem hemitartrate Form E, its composition, and method of use.

IIIa. Claims 232-234, drawn to the process of making Form E.

IV. Claims 144-145, 173-178, and claims 141, 143, 147, 148, 247-258 in part, drawn to Zolpidem hemitartrate Form F, its composition, and method of use.

IVa. Claim 235, drawn to a process of making Form F.

V. Claims 146, 179-184, and claims 141, 143, 147, 148, 247-258 in part, drawn to Zolpidem hemitartrate Form G , its composition, and method of use.

Va. Claim 236-240, drawn to a process of making Form G.

VI. Claims 185-190, and claims 247-258 in part, drawn to Zolpidem hemitartrate Form H, its composition, and method of use.

VIa. Claims 241-244, drawn to a process of making Form H.

VII. Claims 128, 130, 191-196, and claims 124, 129, 139, 140, 247-258 in part, drawn to Zolpidem hemitartrate Form L , its composition, and method of use.

VIIa. Claims 245, 246, drawn to a process of making Form L.

VIII. Claims 197-222, drawn to an independent general process for making Zolpidem hemitartrate.

XI. Claims 138, 259, 260, and claims 137, 247-258 in part, drawn to a Zolpidem hemitartrate Form A.

The claims for the elected Form D are 126-127, 142, 161-166. Generic claims 124, 125,139-141, 143, 147, 148, 247-258 will be examined to the extent that they read on the elected species.

Applicant contends that claims 197-208, 211-212, 215 read on the elected species. However, the *independent process of making Zolpidem hemitartrate* does not have the same scope of any of the compound claims. These claims as recited belongs to a different group, i.e. Group VIII, which in the original election/restriction requirement corresponds to claims 66-89 of Group VIII.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 248-250, 252-254, 256-258 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The non-solvate Form A, B, C, H, L of claims 252-254 have no antecedent basis in the base claim 141, which is drawn to a zolpidem hemitartrate solvate.

b. The non-hydrate Form B, C, F, G, H of claims 248-250 have no antecedent basis in the base claim 124, which is drawn to a zolpidem hemitartrate hydrate.

c. The non-anhydrous Form A, B, D, E, F, G, H, L of claims 256-258 have no antecedent basis in the base claim 149, which is drawn to an anhydrous zolpidem hemitartrate.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 124-127, 14, 142, 166, are rejected under 35 U.S.C. 103(a) as being unpatentable over Ettema I (6281360) in view of Ettema II (6242460, PTO-1449).

Ettema I generically discloses an imidazopyridine derivative with hypnotic and anti-anxiolytic activity (column 5, formula I; column 9, lines 7-10). A specific example, Zolpidem hemitartrate, is described (column 10, example 6).

While Ettema's example is not a monohydrate as recited in instant claims 126-127 or a hemiethanolate of instant claim 142, Ettema teaches that the Zolpidem salt can be in the form of a hydrate or a solvate (column 8, lines 49-50). Ettema II specifically teaches Zolpidem salt in the form of monohydrate (column 11, Example 7) or hemiethanolate (column 11, Example 9) with enhanced stability and is useful in the preparation of pharmaceutical composition for inducing sleep (column 3, lines 24-29).

At the time of the invention, guided by the teachings of Ettema I and II, one of ordinary skill in the art would be motivated to prepare the more stable monohydrate or hemiethanolate form of Zolipdem hemitartrate to arrive at the instant invention.

6. Claims 139, 140, 147, 148, 247-258, are rejected under 35 U.S.C. 103(a) as being unpatentable over Ettema I (6281360) in view of Ettema II (6242460, PTO-1449) and further in view of Lee (5271944, PTO-1449) and/or Bernini (4332721, PTO-1449).

Ettema I or II does not describe the particle size of up to 200 microns as in the instant claims. However, it is well recognized in the art that micronization of crystalline compound would enhance the effectiveness of the drug compound, as expressly taught by Lee for microparticles of from about 5-40 microns (column 2, lines 2-8; lines 28-32) and by Bernini (column 1, lines 42-47).

At the time of the invention, one of ordinary skill in the art would be motivated micronize the Zolpidem hemitartrate hydrate or solvate as taught by Lee and/or Bernini to arrive at the instant invention with the reasonable expectation to achieve enhanced effectiveness of the drug.

7. Claims 124-127, 141, 142, 166 are rejected under 35 U.S.C. 103(a) as being unpatentable over Benincasa (5891891, PTO-1449) in view of Kaplan (4382938, PTO-1449) and Wall, 'Pharmaceutical applications of drug crystal studies', PTO-1449).

Benincasa discloses Zolpidem hemitartrate for the treatment of insomnia (column 2, lines 26-30).

Benincasa does not describes the hydrate or solvate, such as hemiethanolate, as recited in the instant claims.

However, changing the form, purity or other physical characteristic of an old product does not render the new form patentable where the difference in form, purity or characteristic is inherent or rendered obvious by the prior art. In re Cofer 148 USPQ 268. Furthermore, it is well known in the art that different crystalline forms would lead to different physical and chemical properties for development of a better drug, as expressly taught by Wall (page 33, first paragraph). The incorporation of water would lead to hydrate and the incorporation of a solvent would lead to a solvate (page 34, first paragraph). Kaplan teaches the preparation of Zolpidem and related compounds (columns 1-2). The crystallization of the compound in ethanol has been exemplified (column 3, lines 7-8).

At the time of the invention, one of ordinary skill in the art would be motivated to prepare the hydrate or the solvate of Zolpidem as taught by Kaplan and wall to arrive at the instant invention with the reasonable expectation of obtaining the more desirable crystalline hydrate or solvate form of Zolpidem.

8. Claims 139, 140, 147, 148, 247-258, are rejected under 35 U.S.C. 103(a) as being unpatentable over Benincasa (5891891, PTO-1449) in view of Kaplan (4382938, PTO-1449) and Wall, 'Pharmaceutical applications of drug crystal studies', PTO-1449) and further in view of Lee (5271944, PTO-1449) and/or Bernini (4332721, PTO-1449).

Benincasa or Kaplan does not describe the particle size of up to 200 microns as in the instant claims. However, it is well recognized in the art that micronization of crystalline compound would enhance the effectiveness of the drug compound, as expressly taught by Lee for microparticles of from about 5-40 microns (column 2, lines 2-8; lines 28-32) and by Bernini (column 1, lines 42-47).

At the time of the invention, one of ordinary skill in the art would be motivated micronize the Zolpidem hemitartrate hydrate or solvate as taught by Lee and/or Bernini to arrive at the instant invention with the reasonable expectation to achieve enhanced effectiveness of the drug.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 165, 247-258 are rejected under 35 U.S.C. 102(b) as being anticiapated by Benincasa (5891891, PTO-1449). Benincasa's pharmaceutical composition comprising Zolpidem hemitartrate (column 2, lines 15-25) would be the same as the instant composition

comprising a Zolpidem hemitartrate Form D hydrate or solvate, since the optionally micronized hydrate or solvate form of the instant would no longer exist in solution.

Allowable Subject Matter

10. Claims 161-164 are allowed.

While Zolpidem hemitartrate in the form of hydrate or solvate is described by Ettema I and II, Form D with the specific X-ray powder diffraction pattern as recited in the instant claims is not taught or suggested by the prior art of record.

Drawings

11. New corrected drawings are required in this application. See PTO-948. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 703-305-7247. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Evelyn Huang
Primary Examiner
Art Unit 1625

September 28, 2002